CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

74657

CHEMISTRY REVIEW(S)

APPROVAL SUMMARY

ANDA Number: 74-657

FIRM: Invamed Inc. DOSAGE FORM: Terazosin Tablets

STRENGTH 1 mg, 2 mg, 5 mg and 10 mg.

CGMP STATEMENT/EER UPDATE STATEMENT:

All firms on EER were found acceptable on 8/4/99.

BIO STUDY:

Bio found in-vivo and in-vitro data satisfactory on 2/15/96.

Since there is no USP monograph for this product, Bio's dissolution test and specification will be used as the official method.

Dissolution should be conducted in 900 mL of water at 37°C using apparatus II (paddle) at 50 rpm.

NLT % of the labeled amount of Terazosin hydrochloride in the dosage form is dissolved in 30 minutes.

METHODS VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM)

The PHI-DOs worksheet described a batch of drug substance (lot D405168) as a "white powder."

The 1-mg tablet is described as White round tablet marked "INV/256" for lot D941203. It had a drawing which looked like this, ⊖, with INV above the line and 256 below the line. The description in the executed batch record for lot C941203 for the upper punch says: "Embossed INV above the bisect and 256 below the bisect" (see page 002006, Vol. 1.4). The description of MV tablets is the same as in the application.

PHI-DO lab encountered no problems with validation. The Acting District Director on 11/14/96 signed the validation package.

STABILITY - ARE THE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION

The four pilot batches were tested in the smallest (60 cc HPDE bottles with a 33 mm polypropylene screw cap, induction seal liner & cotton coil) containing 100 tablets each and the largest (300 cc HDPE bottles with a 45 mm polypropylene screw cap, induction seal liner and cotton coil) containing 1000 tablets. The containers used in the stability studies were identical to the containers described in Invamed's container section. Three months accelerated stability (40°C/75% RH) data for all 4 lots were satisfactory.

LABELING:

All labeling was found acceptable on 10/29/96.

STERILIZATION VALIDATION (IF APPLICABLE): N/A

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.)

The size of lot D941201, which was the 5-mg bio batch is tablets. NDS was satisfactory. The NDS is OK. DMF is adequate.

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED BY THE SAME PROCESS?)

The sizes of the 1 mg (lot D 941203), 2 mg (D 941204) and 10 mg (lot D 94205) tablets were tablets each.

PROPOSED PRODUCTION BATCHES - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?

All production batches tablets.

The manufacturing process of proposed production batches are the same as was used for the bio-batch.

Prepared by Stephen Sherken on 4/11/00.

Review Chemist: S.Sherken /S/ 4/12/00 Date: 4/12/00

Team Leader: D.Gill /S/ 4-24-00 Date: 4/14/00

1. CHEMISTRY REVIEW NO 5

2. ANDA 74-657

3. NAME AND ADDRESS OF APPLICANT

Invamed, Inc.
Dayton, NJ 08810

4. LEGAL BASIS FOR SUBMISSION

505(j)

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

None

7. NONPROPRIETARY NAME

Terazosin Hydrochloride (anhydrous).

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

DOA 4/8/95; RTF 4/24/95; Amend 4/29/85; AFF 5/19/95 (Acceptable for filing) NC 5/1/95; NC 5/3/95; NC 6/11/95; NA 11/22/95; NC 12/8/95; Amend 12/21/95; Amend 4/12/96; NA 5/14/96; Amend (Minor) 7/15/96; Memo of Telephone Conversation 8/12/96; Telephone Amendment 8/12/96; Control Doc 8/26/96; Label Amend 9/6/96; Label Rev 9/23/96; NC 9/25/96; Label Amend 10/12/96; Label Review 10/24/96; Tel- Amend 11/22/96; NC 12/23/96 (Paragraph IV); Tentative Approval Letter to Invamed 3/7/97; NC (Paragraph IV) 9/25/97; NC 10/1/97; NC 10/31/97; NC (Abbott) 9/28/98; NC (Patent amend) 9/30/98; NC 10/20/98; Amendment (Minor) 7/15/99; Tel amendment (Certifies that there are no changes being implemented in labeling, chemistry, manufacturing & controls) 7/23/99; Tel amend (Identified three testing labs and drug substance manufacturer & supplier) 7/24/99; Tentative Approval letter to Invamed; Minor Amend to Tentatively Approved ANDA 3/25/00; NC 3/28/00.

10. PHARMACOLOGICAL CATEGORY

Benign Prosthetic Hyperplasia

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF
DMF

13. DOSAGE FORM

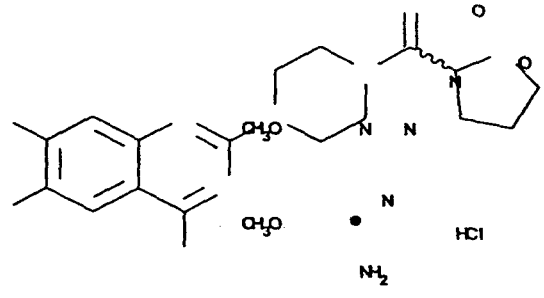
14. POTENCY

White, unscored, round, tablets, engraved INV & 324 on one side.	1 mg*
Beige, unscored, round, tablets, engraved INV & 325 on one side.	2 mg*
Pink, unscored, round, tablets, engrave INV & 326 on one side.	5 mg*
Yellow, unscored, round, tablets, engraved INV & 327 on one side.	10 mg*

- as Terazosin base (anhydrous)
-

15. CHEMICAL NAME AND STRUCTURE

Terazosin Hydrochloride
C19H25N5O4.HCL; M.W. = 423.90



1-(4-Amino-6,7-dimethoxy-2-quinazolinyl)-4-(tetrahydro-2-furoyl)piperazine monohydrochloride.
[63074-08-8]

16. RECORDS AND REPORTS

N/A

17. COMMENTS

A minor amendment dated March 25, 2000 certifies that Invamed has made no changes in the labeling, chemistry, manufacturing and controls for Terazosin Tablets.

Bio found in-vivo and in-vitro data satisfactory on 2/20/96.

Labeling remains adequate.

All analytical methods were satisfactorily validated by the PHI-DO on 11/14/96.

EER found acceptable by M. Egas on 04-AUG-1999.

DMF found adequate on 2/10/00.

18. CONCLUSIONS AND RECOMMENDATIONS

DMF is adequate and ANDA 74-657 should be approved.

RECOMMENDATION - Approve ANDA 74-657.

19. REVIEWER: DATE COMPLETED:

STEPHEN SHERKEN April 12, 2000

cc: ANDA 74-657
Division File
Field Copy

Endorsements:
HFD-623/S.Sherken/4-12-00 /S/ 4/19/00
HFD-623/D.Gill/4-14-00 /S/ 4-24-00

Approval

Redacted 7

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information

Chem. Review #5